HTT gene

huntingtin

Normal Function

The *HTT* gene provides instructions for making a protein called huntingtin. Although the exact function of this protein is unknown, it appears to play an important role in nerve cells (neurons) in the brain and is essential for normal development before birth. Huntingtin is found in many of the body's tissues, with the highest levels of activity in the brain. Within cells, this protein may be involved in chemical signaling, transporting materials, attaching (binding) to proteins and other structures, and protecting the cell from self-destruction (apoptosis).

One region of the *HTT* gene contains a particular DNA segment known as a CAG trinucleotide repeat. This segment is made up of a series of three DNA building blocks (cytosine, adenine, and guanine) that appear multiple times in a row. Normally, the CAG segment is repeated 10 to 35 times within the gene.

Health Conditions Related to Genetic Changes

Huntington disease

The inherited mutation that causes Huntington disease is known as a CAG trinucleotide repeat expansion. This mutation increases the size of the CAG segment in the *HTT* gene. People with Huntington disease have 36 to more than 120 CAG repeats. People with 36 to 39 CAG repeats may or may not develop the signs and symptoms of Huntington disease, while people with 40 or more repeats almost always develop the disorder.

The expanded CAG segment leads to the production of an abnormally long version of the huntingtin protein. The elongated protein is cut into smaller, toxic fragments that bind together and accumulate in neurons, disrupting the normal functions of these cells. This process particularly affects regions of the brain that help coordinate movement and control thinking and emotions (the striatum and cerebral cortex). The dysfunction and eventual death of neurons in these areas of the brain underlie the signs and symptoms of Huntington disease.

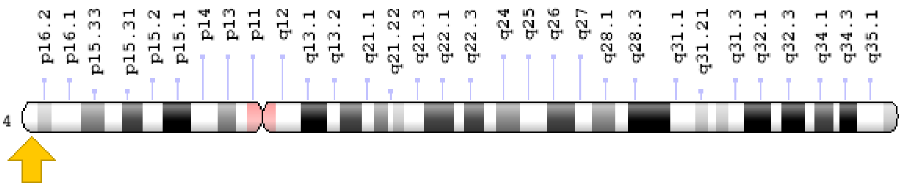
As the altered *HTT* gene is passed from one generation to the next, the size of the CAG trinucleotide repeat often increases in size. A larger number of repeats is usually associated with an earlier onset of signs and symptoms. This phenomenon is called anticipation. People with the adult-onset form of Huntington disease (which appears in mid-adulthood) typically have 40 to 50 CAG repeats in the *HTT* gene, while people with the less common, juvenile form of the disorder (which appears in childhood or adolescence) tend to have more than 60 CAG repeats.

Individuals who have 27 to 35 CAG repeats in the *HTT* gene do not develop Huntington disease, but they are at risk of having children who will develop the disorder. As the gene is passed from parent to child, the size of the CAG trinucleotide repeat may lengthen into the range associated with Huntington disease (36 repeats or more).

Chromosomal Location

Cytogenetic Location: 4p16.3, which is the short (p) arm of chromosome 4 at position 16.3

Molecular Location: base pairs 3,074,510 to 3,243,960 on chromosome 4 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- HD
- HD_HUMAN
- huntingtin (Huntington disease)
- Huntington's disease protein
- IT15

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Some Genetic Diseases Are Caused by the Expansion of Repeats of Three Nucleotides https://www.ncbi.nlm.nih.gov/books/NBK22525/#A3843

GeneReviews

- Huntington Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1305

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28HD%5BTI%5D%29+OR+%28huntingtin%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- HUNTINGTIN
  http://omim.org/entry/613004

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_HTT.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HTT%5Bgene%5D
- HGNC Gene Family: Endogenous ligands
  http://www.genenames.org/cgi-bin/genefamilies/set/542
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4851
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3064
- UniProt
  http://www.uniprot.org/uniprot/P42858

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